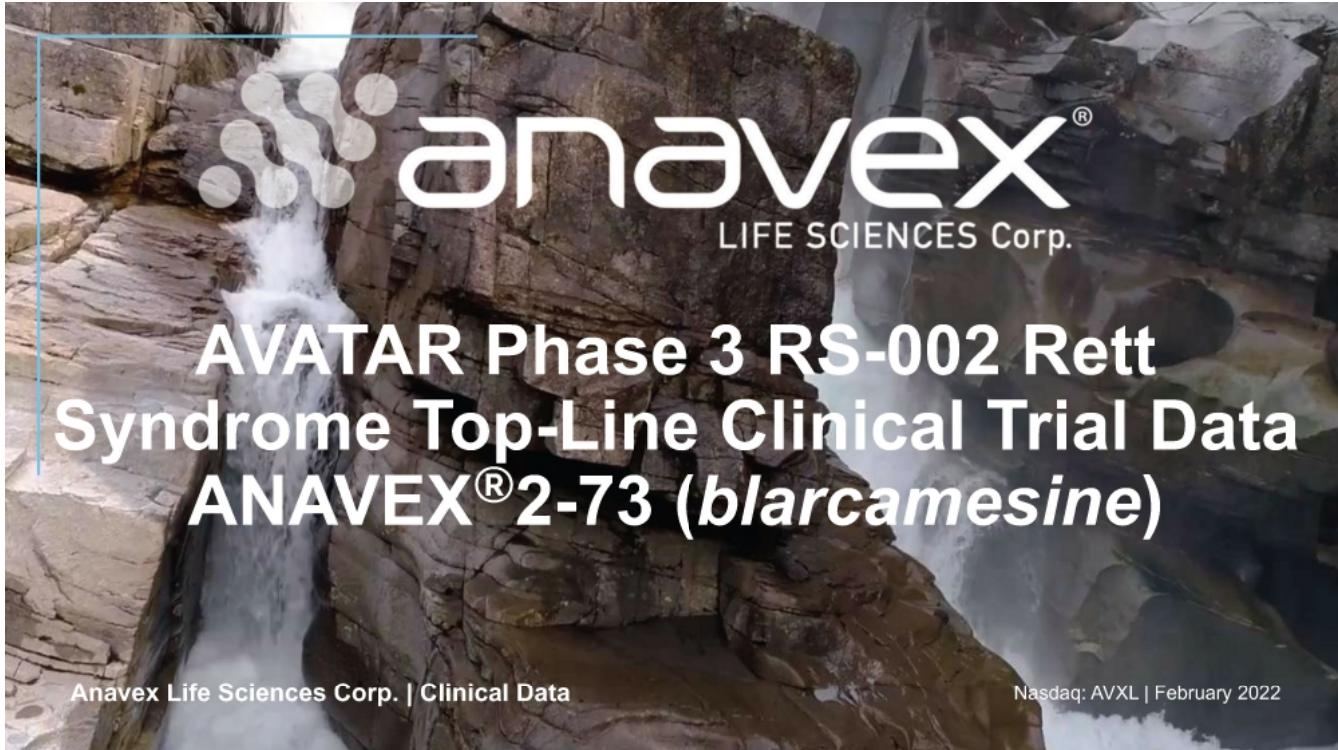


# Exhibit 5



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LIFE SCIENCES Corp.

**AVATAR Phase 3 RS-002 Rett Syndrome Top-Line Clinical Trial Data ANAVEX®2-73 (*blarcamesine*)**

Anavex Life Sciences Corp. | Clinical Data Nasdaq: AVXL | February 2022

## Forward Looking Statement

This presentation contains forward-looking statements made within the meaning of the Private Securities Litigation Reform Act of 1995 by Anavex® Life Sciences Corp. and its representatives. These statements can be identified by introductory words such as "expects," "plans," "intends," "believes," "will," "estimates," "forecasts," "projects," or words of similar meaning, and by the fact that they do not relate strictly to historical or current facts. Forward-looking statements frequently are used in discussing potential product applications, potential collaborations, product development activities, clinical studies, regulatory submissions and approvals, and similar operating matters. Many factors may cause actual results to differ from forward-looking statements, including inaccurate assumptions and a broad variety of risks and uncertainties, some of which are known and others of which are not. Known risks and uncertainties include those identified from time to time in reports filed by Anavex Life Sciences Corp. with the Securities and Exchange Commission, which should be considered together with any forward-looking statement. No forward-looking statement is a guarantee of future results or events, and one should avoid placing undue reliance on such statements. Anavex Life Sciences Corp. undertakes no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise. Anavex Life Sciences Corp. cannot be sure when or if it will be permitted by regulatory agencies to undertake clinical trials or to commence any particular phase of any clinical trials. Because of this, statements regarding the expected timing of clinical trials cannot be regarded as actual predictions of when Anavex Life Sciences Corp. will obtain regulatory approval for any "phase" of clinical trials. We also cannot be sure of the clinical outcome for efficacy or safety of our compounds. Potential investors should refer to the risk factors in our reports filed on Edgar.

# What is Rett Syndrome?

Devastating Neuro-developmental Disease in Girls with both Movement Impairment and Cognitive Impairment

## Rett Syndrome (RTT)

- Non-inherited genetic postnatal disorder caused by mutations in the MECP2 gene
  - Occurs almost exclusively in girls
  - Leads to severe impairments, affecting nearly every aspect of the child's life
  - Impairment includes ability to speak, walk, eat and even breathe easily
  - Hallmark of RTT is near constant repetitive hand movements while awake
  - Occurs worldwide in approximately one in every 10,000 to 15,000 live female births
  - The population of patients with Rett syndrome is estimated to be ~11,000 patients in the U.S.
  - There is currently no cure for Rett syndrome

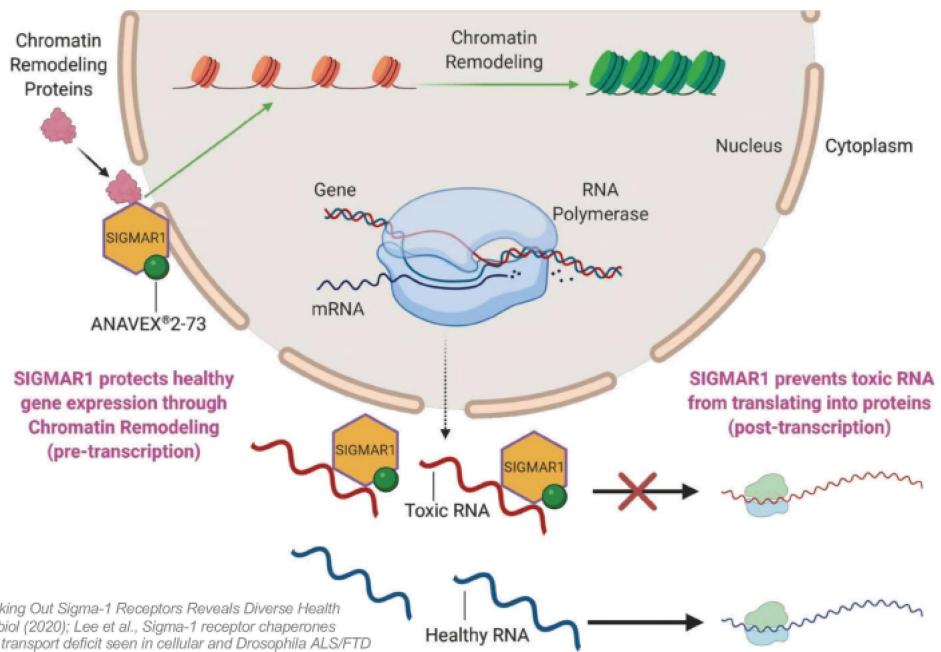


Source: <https://www.rettsyndrome.org/about-rett-syndrome>

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## ANAVEX®2-73 MoA: SIGMAR1 Activation Prevents Cellular Stress Before and After Gene Transcription



Source: Couly et al., Knocking Out Sigma-1 Receptors Reveals Diverse Health Problems. *Cell Mol Neurobiol* (2020); Lee et al., Sigma-1 receptor chaperones rescue nucleocytoplasmic transport deficit seen in cellular and *Drosophila* ALS/FTD models. *Nat Commun*. 2020 Nov 4;11(1):5580

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## ANAVEX® Rett Syndrome Program

### Completed and ongoing late-stage clinical studies for Rett Syndrome in 2022:

- U.S. Phase 2 Adult Rett Syndrome Trial (ClinicalTrials.gov Identifier: NCT03758924) - *completed*
- AVATAR Phase 3 Adult Rett Syndrome Trial (ClinicalTrials.gov Identifier: NCT03941444) - *completed*
- EXCELLENCE Phase 2/3 Pediatric Rett Syndrome Trial (ClinicalTrials.gov Identifier: NCT04304482) - *ongoing*
- ANAVEX®2-73 Rett Syndrome Program Received **Fast Track** Designation, **Orphan Drug** Designation and **Rare Pediatric Disease** Designation

Pivotal Efficacy	Supportive Efficacy	Safety Database
<ul style="list-style-type: none"> <li>Positive Phase 3 AVATAR Study</li> </ul>	<ul style="list-style-type: none"> <li>Positive Phase 2 U.S. Rett Syndrome Study</li> </ul>	<ul style="list-style-type: none"> <li>Safety and Tolerability Data from Completed &amp; Ongoing Studies</li> </ul>

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### Phase 3 AVATAR ANAVEX®2-73-RS-002 Trial in Adult Patients with Rett Syndrome - Design Overview

Randomized, Double-blind, Placebo-controlled Multi-center Clinical Trial



#### Assessments:

- Primary: Assessment of RSBQ AUC response and safety
- Secondary: Emotional behavior (ADAMS) response and CGI-I (Clinical Global Impression of Improvement) response
- Exploratory: Sleep (CSHQ), VAS (top caregiver concerns), Child Health Questionnaire PF50 (CHQ-PF50), Rett syndrome Caregiver Inventory Assessment (RTT-CIA), Seizure diary
- Biomarkers of response and/or surrogate endpoints: DNA & mRNA profiles and metabolomics biomarkers
- SIGMAR1* variants: Prespecified analyses of population with wild type (WT) variant

ClinicalTrials.gov: NCT03941444

Separate patient cohort (n=3) underwent a 3-week intensive pharmacokinetic (PK) assessment with safety, tolerability, pharmacokinetic and efficacy evaluation of ANAVEX®2-73

Open-label-extension (OLE) after End of Trial for at least 48 weeks

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## Baseline Characteristics

	ANAVEX®2-73 (n=20)	PLACEBO (n=13)	TOTAL (n=33)
Age (years) – Median	24.8	23.6	24.3
Range - Min, Max	18.20, 38.35	19.53, 40.78	18.20, 40.78
Weight (kg) – Median	41.6	54.8	46.8
Range - Min, Max	33.0, 76.0	29.0, 84.0	29.0, 84.0
Baseline AED medications, %	80%	85%	82%
Baseline CGI-S Category, n (%)			
4-Moderately Ill	5 (25%)	4 (31%)	9 (27%)
5-Markedly Ill	11 (55%)	6 (46%)	17 (52%)
6-Severely Ill	4 (20%)	3 (23%)	7 (21%)
7-Extremnely Ill	0 (0%)	0 (0%)	0 (0%)

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## Appropriate Primary Endpoint for Rett Syndrome

### Background for Pivotal Trial Endpoint

- Statistical significance alone not sufficient for determining whether an individual patient has experienced a meaningful clinical benefit
- As a *stand-alone* caregiver reported primary outcome assessment, the RSBQ does not appear optimally suited, on its own, for the determination of a clinical trial outcome (e.g., could lead to either type 1 or type 2 error)<sup>1</sup>
- FDA:
  - **Anchor-based responder method**<sup>2</sup> – linking of scores from one clinical outcome assessment (e.g., RSBQ)<sup>3</sup> with scores from a simple reference “anchor” clinical outcome assessment with a **clinically meaningful threshold** (e.g., CGI-I)<sup>4</sup> to facilitate interpretation of what constitutes a meaningful within and between patient change in clinical outcome assessment scores (e.g., RSBQ AUC)<sup>5</sup>

1) Hou W, Bhattacharya U, Pradana WA, Tarquinio DC. Assessment of a Clinical Trial Metric for Rett Syndrome: Critical Analysis of the Rett Syndrome Behavioural Questionnaire. *Pediatr Neurol*. 2020 Jun;107:48-56. doi: 10.1016/j.pediatrneurol.2020.01.009. Epub 2020 Feb 4. PMID: 32165033

2) Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims>

3) Rett Syndrome Behavioural Questionnaire

4) Clinical Global Impression of Improvement

5) Area Under the Effective Curve to account for drug exposure over the course of duration of the trial

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## Primary Endpoint for Phase 3 AVATAR Clinical Trial for Adult Patients with Rett Syndrome

### Capturing Clinically Meaningful Treatment Effect and Disease Progression

- The RSBQ AUC (area under the effect curve) is a summary measure that combines both **treatment effect and disease progression** into one composite score
- It captures not only the end of treatment effect, but also the progression of the disease over the course of the study with better precision than only an end of treatment score<sup>1</sup>
- **CGI-I** (Clinical Global Impression of Improvement) **anchored RSBQ AUC score: Improvement threshold** of at least 1 full point in the 7-point scale from 'No Change' (i.e., 4) to at least 'Minimally Improved' (i.e., 3) or 'Much Improved' (i.e., 2) or 'Very Much Improved' (i.e., 1)
- **Responder** is defined as a study participant who **exceeds the clinically meaningful CGI-I threshold with corresponding RSBQ AUC linked value** indicating improvement
- CGI-I anchored RSBQ AUC has been previously successfully assessed as efficacy endpoint in U.S. Rett Syndrome ANAVEX®2-73-RS-001 trial

<sup>1</sup> Pham B, Cranney A, Boers M, Verhoeven AC, Wells G, Tugwell P. Validity of area-under-the-curve analysis to summarize effect in rheumatoid arthritis clinical trials. *J Rheumatol*. 1999;26(3):712-716.

## CGI-I Scale

### Clinical Global Impression of Improvement (CGI-I)

The Clinical Global Impression of Improvement Scale (CGI-I) is a measure developed for use in clinical trials to provide a brief, stand-alone assessment of the clinician's view of the patient's global functioning prior to and after initiating a study medication. Each time the patient is seen after medication has been initiated, the clinician compares the patient's overall clinical condition to the period just prior to the initiation of medication use (the so-called baseline visit).<sup>1</sup>

- Mimics what a physician would do in practice if an intervention is helping
- Measure both global and individual domain ratings like CGI-S (Clinical Global Impression of Severity)
- CGI-I measures clinical change in a "Very Much Worse" (7 score) to "Very Much Improved" (1 score) range
- The CGI-S score obtained at the baseline (initiation) visit serves as a good basis for making this assessment. The following question is rated on a seven-point scale: "Compared to the patient's condition at admission to the project [prior to medication initiation], this patient's condition is: 1=very much improved since the initiation of treatment; 2=much improved; 3=minimally improved; 4=no change from baseline (the initiation of treatment); 5=minimally worse; 6=much worse; 7=very much worse since the initiation of treatment."
- Only scores of 1 or 2 or 3 are defined as treatment "responders"
- Score of 3 or less represent clearly observable clinically meaningful manifestation of drug effect
- This implies that the minimal important difference is a change of 1 unit from a CGI-I of 4 (no change) to a CGI-I of 3 (minimal improvement)

Clinically Meaningful						
✗	✗	✗	✗	✓	✓	✓
7	6	5	4	3	2	1

Very Much Worse	Much Worse	Minimally Worse	No Change	Minimally Improved	Much Improved	Very Much Improved
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<sup>1</sup> Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry (Edgmont)*. 2007;4(7):28-37.

# ADAMS Scale

## Anxiety, Depression, and Mood Scale (ADAMS)

The Anxiety, Depression, and Mood Scale (ADAMS) is a measure of anxiety and mood symptoms in individuals with intellectual disability.<sup>1</sup> It has been clinically validated for use in Rett syndrome<sup>2</sup> and in Fragile X syndrome<sup>3</sup>

The ADAMS generates a total score and 5 subscale scores:

- Manic/hyperactive behavior
- Depressed mood
- Social avoidance
- General anxiety
- Obsessive compulsive behavior

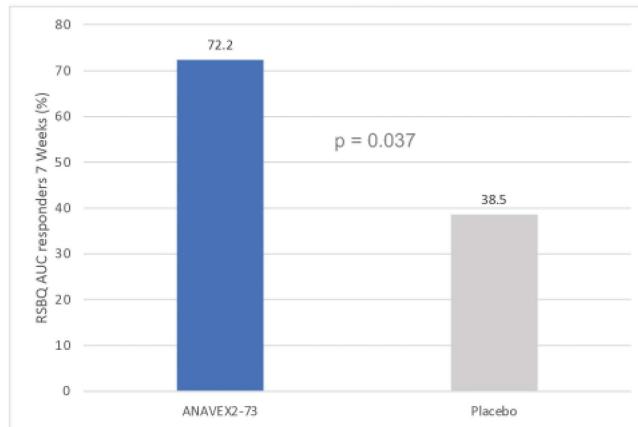
1) Esbensen AJ, Rojahn J, Aman MG, Ruedrich S. Reliability and validity of an assessment instrument for anxiety, depression, and mood among individuals with mental retardation. *J Autism Dev Disord*. 2003;33:617–29 Kluwer Academic Publishers-Plenum Publishers.  
 2) Barnes KV, Coughlin FR, O'Leary HM, Bruck N, Bazin GA, Beinecke EB, Walco AC, Cantwell NG, Kaufmann WE. Anxiety-like behavior in Rett syndrome: characteristics and assessment by anxiety scales. *J Neurodev Disord*. 2015;7(1):30. doi: 10.1186/s11689-015-9127-4. Epub 2015 Sep 15.  
 3) Cordeiro L, Ballinger E, Hagerman R, Hessl D. Clinical assessment of DSM-IV anxiety disorders in fragile X syndrome: prevalence and characterization. *J Neurodev Disord*. 2011;3:57–67. doi: 10.1007/s11689-010-9067-y. Epub 2010 Dec 3.

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# Primary Endpoint

## Primary Efficacy Endpoint



- ANAVEX®2-73 induces a clinical meaningful improvement of RSBQ AUC\* in 72.2% of patients as compared to 38.5% on placebo; (p = 0.037)
- Cohen's d effect size 1.91 (very large)

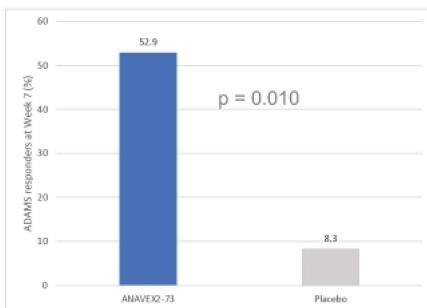
\*Improvement threshold of at least 1 full point in the CGI-I scale from 'No Change' (i.e., 4) to at least 'Minimally Improved' (i.e., 3) or 'Much Improved' (i.e., 2) or 'Very Much Improved' (i.e., 1)

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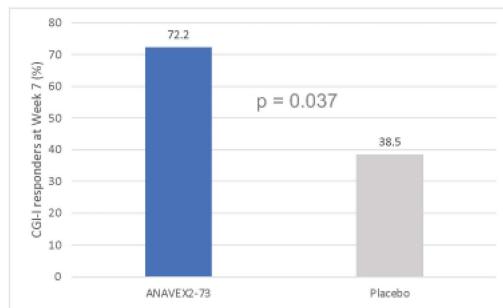
## Secondary Endpoints

### Secondary Efficacy Endpoints ADAMS and CGI-I



- Clinically meaningful and statistically significant reduction of emotional behavioral symptoms (ADAMS) response\* for ANAVEX®2-73 treated adult patients with Rett syndrome (52.9%) vs placebo (8.3%); (p = 0.010)
- Cohen's d effect size 0.609 (large)

\* Improvement threshold of at least -20% change (improvement) of ADAMS total score from baseline



- Significantly more patients achieve clinically meaningful CGI-I response\*\* over the treatment duration in ANAVEX®2-73-treated group (72.2%) as compared with placebo (38.5%); (p = 0.037)
- Cohen's d effect size 1.91 (very large)

\*\* Improvement threshold of at least 1 full point in the CGI-I scale from 'No Change' (i.e., 4) to at least 'Minimally Improved' (i.e., 3) or 'Much Improved' (i.e., 2) or 'Very Much Improved' (i.e., 1)

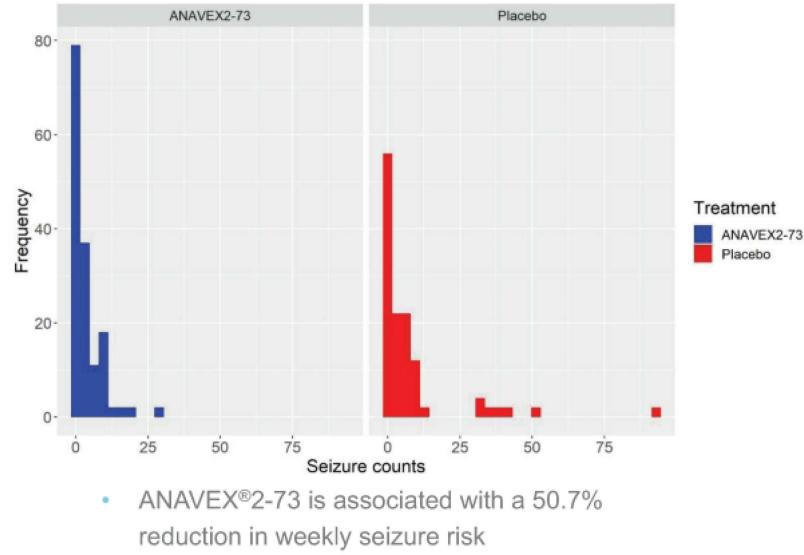
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## Other Endpoints

### Quality of Life (QoL) Assessment and Distribution of Seizure Count by Treatment Arm

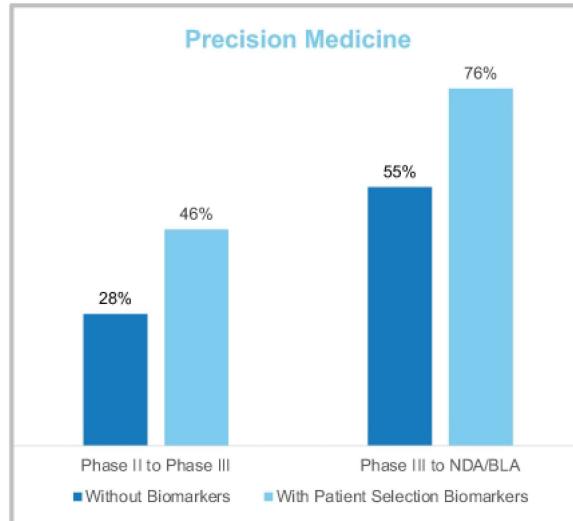
- Child Health Questionnaire-Parent Form 50 (CHQ-PF50)
- The CHQ-PF50 is an internationally recognized general health-related global measure of Quality of Life (QoL) encompassing physical and psychosocial concepts (physical function, psychosocial, behavior, bodily pain, emotional impact, family activities, family cohesion, and general health perception)
- ANAVEX®2-73 demonstrated dose-related significant improvement in overall Quality of Life (QoL) measured with CHQ-PF50 Total Score (p = 0.030)



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## Biomarkers Increase Probability of Success



- Patient selection biomarkers
- Higher therapeutic response
- Lower variability in the target population

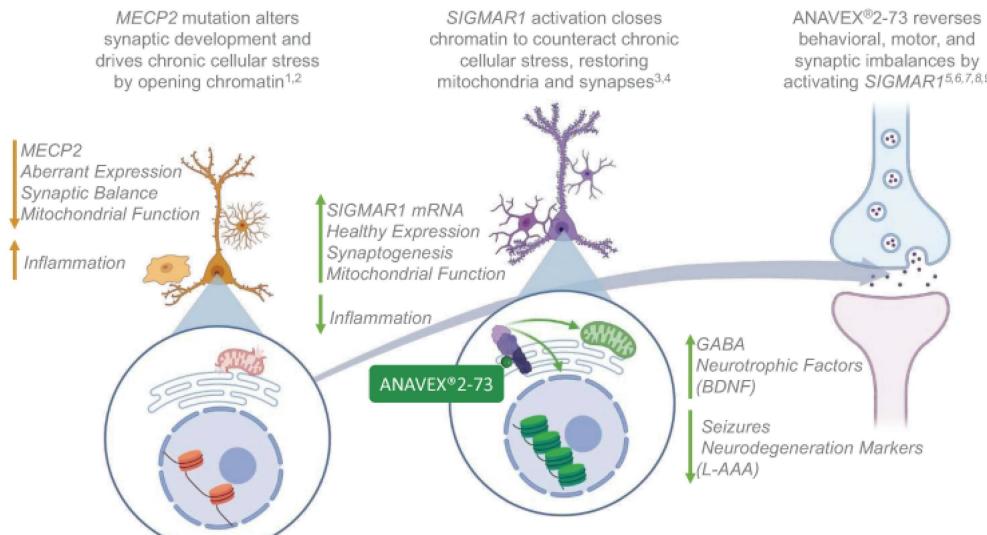
Thomas DW et al. Clinical Development Success Rates 2006-2015. BIO Industry Analysis

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## ANAVEX®2-73 Mechanism of Action for Rett Syndrome

### SIGMAR1 Activation is Beneficial in Restoring Neuronal Homeostasis



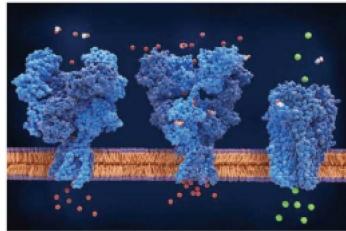
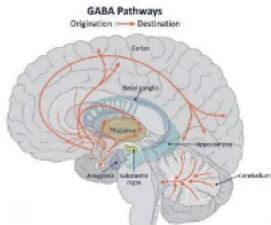
1) Li et al., 2020; 2) Wang et al., 2020; 3) Crouzier et al., 2020; 4) Lee et al., 2020; 5) Kaufmann et al., 2019; 6) Kaufmann et al., 2019b; 7) Lahmy et al., 2015; 8) Lisak et al., 2020; 9) ANAVEX2-73-RS-002 Data

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## GABA a Potential Biomarker, Predicting Clinical Outcome in ANAVEX®2-73 Rett Syndrome Study

- In patients with RTT, *MECP2* deficiency disrupts the GABAergic cycle<sup>1</sup>, resulting in **decreased** GABA, and impaired synaptic and mitochondrial function<sup>1,2,3,4,5,6</sup>



- AVATAR efficacy endpoints demonstrated statistically significant and clinically meaningful reductions in Rett syndrome symptoms with related changes in potential biomarkers of disease pathology:
- GABA<sup>7</sup> was significantly **increased** ( $p = 0.0205$ )
- Gliotoxin L-Alpha-aminoacidic acid (L-AAA)<sup>8</sup> was significantly **decreased** ( $p = 0.0392$ )

1) Jin et al., 2015; 2) Chao et al., 2020; 3) Hamberger et al., 1992; 4) Lappalainen et al., 1996; 5) Neul et al., 2020 6) Kaufmann et al., 2005  
7) Ure K, Lu H, Wang W, et al. Restoration of *Mecp2* expression in GABAergic neurons is sufficient to rescue multiple disease features in a mouse model of Rett syndrome. *Elife*. 2016 Jun 21;5:e14198; 8) Wu HQ, Ungerstedt U, Schwarcz R. L-alpha-aminoacidic acid as a regulator of kynurenic acid production in the hippocampus: a microdialysis study in freely moving rats. *Eur J Pharmacol*. 1995 Jul 25;281(1):55-61

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## Safety and Adverse Events During Treatment Period

- ANAVEX®2-73 was well tolerated with very good medication compliance of 95%
- Similar TEAE rates observed in ANAVEX®2-73 and placebo arms
- AEs  $\geq 10\%$  were predominantly mild or moderate
- No clinically significant changes in vital signs, lab values and ECG parameters in ANAVEX®2-73 and placebo groups
- No incidence of diarrhea or vomiting
- Safety findings are consistent with the known safety profile of ANAVEX®2-73

Adverse Events During the Treatment Period		
	ANAVEX®2-73 (n=20) number (%)	Placebo (n=13) number (%)
Patients with any TEAE	15 (75.0%)	8 (61.5%)
Patients with a serious TEAE	3 (15.0%)	2 (15.4%)
Patients with a TEAE leading to Study Discontinuation	2 (10.0%)	1 (7.7%)
<b>AEs <math>\geq 10\%</math></b>		
Somnolence <sup>1</sup>	4 (20.0%)	2 (15.4%)
Lethargy <sup>2</sup>	4 (20.0%)	0 (0.0%)
Sedation	2 (10.0%)	0 (0.0%)
Constipation	2 (10.0%)	1 (7.7%)
Urinary tract infection	2 (10.0%)	1 (7.7%)
Hypophagia	2 (10.0%)	0 (0.0%)
Skin rash	2 (10.0%)	1 (7.7%)

<sup>1</sup> Medical history of Somnolence in 3 patients; 1 severe, all others mild

<sup>2</sup> All mild

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## Overall Summary

### Phase 3 AVATAR Clinical Trial for Adult Patients with Rett Syndrome

- Primary (RSBQ AUC;  $p = 0.037$ ) and secondary (ADAMS;  $p = 0.010$ ); (CGI-I;  $p = 0.037$ ) efficacy and safety endpoints met
- Efficacy endpoints demonstrated statistically significant and clinically meaningful reductions in Rett syndrome symptoms with related changes in potential biomarkers of disease pathology:
  - GABA was significantly increased ( $p = 0.0205$ )
  - L-Alpha-aminoacidic acid (L-AAA) was significantly decreased ( $p = 0.0392$ )
- Convenient once daily oral liquid doses of up to 30mg ANAVEX®2-73 were well tolerated without safety concerns identified
- Confirmed dose-response:
  - RS-001 study 5mg ANAVEX®2-73 dose RSBQ AUC Cohen's d (effect size) of 0.517
  - RS-002 study 30mg ANAVEX®2-73 dose RSBQ AUC Cohen's d (effect size) of 1.91
- Analysis of weekly seizure counts indicated that relative to placebo, ANAVEX®2-73 is associated with a 50.7% reduction in weekly seizure risk
- ANAVEX®2-73 demonstrated dose-related significant improvement in overall Quality of Life (QoL) measured with CHQ-PF50 ( $p = 0.030$ )
- Key milestone met to advance regulatory approval pathway for adult patients with Rett syndrome
- Discussing with FDA a pathway for potential approval of ANAVEX®2-73 for adult patients with Rett syndrome

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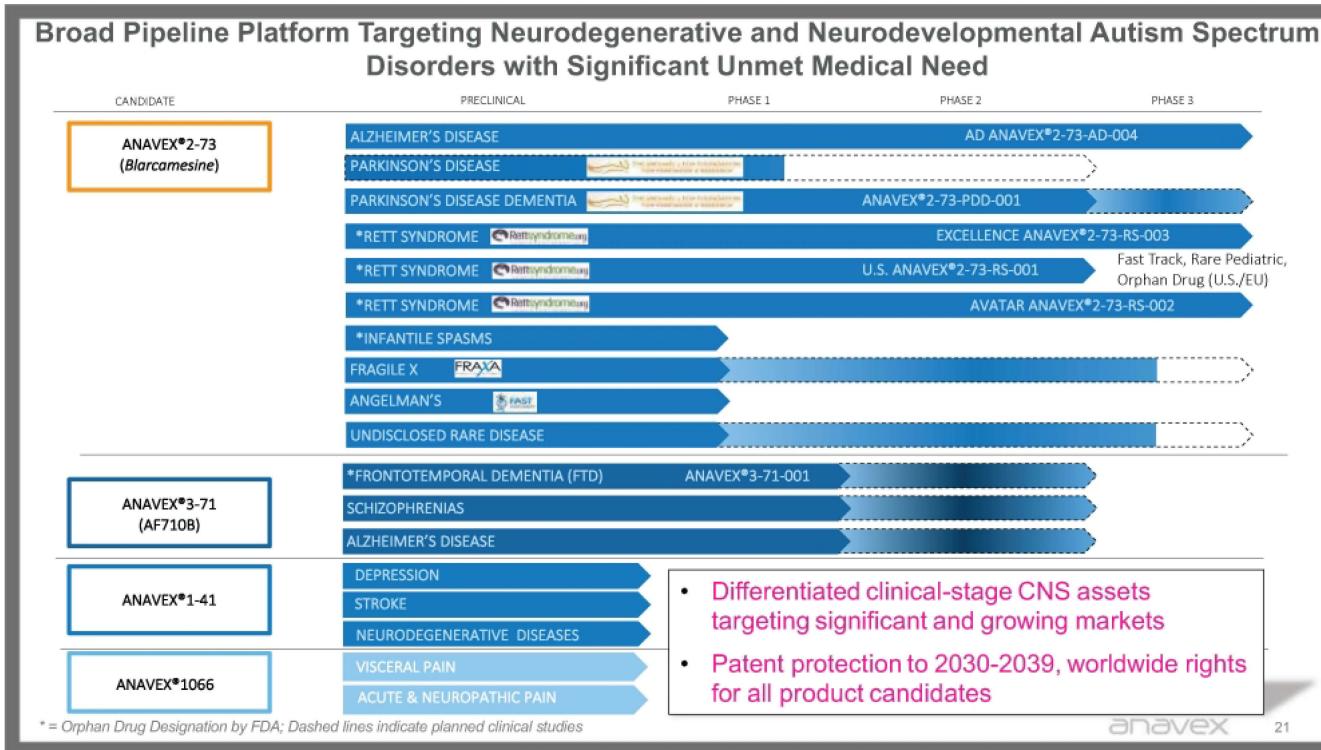
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## Acknowledgments

We thank all the patients and their family members participating in the Rett syndrome ANAVEX®2-73-RS-002 study, as well as the investigators and their staff conducting these studies and the global Rett Syndrome Associations.

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**Anavex is the only Company pursuing Large Markets by Applying Precision Medicine to Develop Treatments for both Global Aging CNS diseases (Alzheimer's, Parkinson's), as well as catastrophic Orphan Genetically caused diseases, Rett Syndrome with High Unmet Needs**

**\$ 277B**

**Economic burden**

2018 Alzheimer's Association

OVERARCHING MESSAGE

A **novel approach is needed** to address the totality of CNS diseases

#### PRECISION MEDICINE PLATFORM IMPROVES CHANCE OF CLINICAL SUCCESS



Testing for biomarkers demonstrated improved clinical response to ANAVEX®2-73 in Rett syndrome, Parkinson's and Alzheimer's patients correlated with mRNA SIGMAR1 gene expression

#### STRONG IP POSITION AROUND NOVEL MECHANISM OF ACTION



ANAVEX®2-73, is an orally available Sigma-1 receptor agonist that has been shown to restore homeostasis (composition of matter patent protection to 2037)

#### COMPELLING HUMAN DATA PLATFORM



ANAVEX®2-73 Phase 3 and Phase 2 in Rett syndrome, Phase 2 Parkinson's disease dementia (PDD) and Phase 2a trial in Alzheimer's disease with favorable safety and exploratory efficacy results through 148 weeks

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# Contact Us

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